DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

BIOFIRE DIAGNOSTICS, LLC
KRISTEN KANACK
VICE PRESIDENT OF REGULATED PRODUCTS
390 WAKARA WAY
SALT LAKE CITY UT 84108

February 17, 2015

Re: K143080
Trade/Device Name: FilmArray Respiratory Panel (RP)
For Use with Multi-instrument FilmArray System
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: II
Product Code: OCC, OEM, OOU, OEP, OTG, OOI, OZX, OZY, OQW, OZZ
Dated: January 15, 2015
Received: January 16, 2015

Dear Dr. Kanack:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
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and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143080

Device Name
FilmArray Respiratory Panel (RP)

Indications for Use *(Describe)*
The FilmArray Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with FilmArray systems for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Human Rhinovirus/Enterovirus, Respiratory Syncytial Virus, Bordetella pertussis, Chlamydophila pneumoniae, and Mycoplasma pneumoniae. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or, lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the Film Array RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for Bordetella pertussis, Coronavirus 229E, Coronavirus OC43, Influenza A H1, Influenza A H3, Influenza A H1-2009, Influenza B, Mycoplasma pneumoniae, Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for Chlamydophila pneumoniae were established primarily using contrived clinical specimens.

Due to the genetic similarity between Human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for Influenza A were established when Influenza A 2009 H1N1, A H1, and A H3 were the predominant Influenza A viruses in circulation. Performance of detecting Influenza A may vary if other Influenza A strains are circulating or a novel Influenza A virus emerges. If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary
BioFire Diagnostics, LLC

FilmArray Respiratory Panel (RP) for use with the FilmArray 2.0 and FilmArray Injection Vials

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitted by:

BioFire Diagnostics, LLC
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Salt Lake City, UT 84108
USA

Telephone: 801-736-6354
Facsimile: 801-588-0507

Contact: Kristen Kanack, ext. 330

Date Submitted: October 24, 2014

Device Name and Classification:

Trade Name: FilmArray Respiratory Panel (RP)

Regulation Number: 21 CFR 866.3980

Classification Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay

Predicate Device:

K123620 – FilmArray Respiratory Panel

Intended Use:

The FilmArray Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with FilmArray systems for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Human Rhinovirus/Enterovirus, Respiratory Syncytial Virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The detection and identification of specific viral and

bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or, lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the Film Array RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Bordetella pertussis*, Coronavirus 229E, Coronavirus OC43, Influenza A H1, Influenza A H3, Influenza A H1-2009, Influenza B, *Mycoplasma pneumoniae*, Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for *Chlamydophila pneumoniae* were established primarily using contrived clinical specimens.

Due to the genetic similarity between Human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for Influenza A were established when Influenza A 2009 H1N1, A H1, and A H3 were the predominant Influenza A viruses in circulation. Performance of detecting Influenza A may vary if other Influenza A strains are circulating or a novel Influenza A virus emerges. If infection with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Device Description:

The FilmArray Respiratory Panel is a multiplex nucleic acid test designed to be used with FilmArray systems. The FilmArray RP pouch contains freeze-dried reagents to perform nucleic acid purification, reverse transcription, and nested, multiplex PCR with DNA melt analysis. FilmArray RP simultaneously conducts 20 tests for the identification of respiratory pathogens from nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections (Table 1). Results from the FilmArray RP test are available within about one hour.

Table 1. Bacteria and Viruses Detected by the FilmArray Respiratory Panel

Viral Respiratory Pathogens
Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
Human Metapneumovirus
Human Rhinovirus/Enterovirus
Influenza A
H1 subtype
H3 subtype
H1-2009 subtype
Influenza B
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus
Bacterial Respiratory Pathogens
Bordetella pertussis
Chlamydophila pneumoniae
Mycoplasma pneumoniae

A test is initiated by loading Hydration Solution and an unprocessed patient nasopharyngeal swab (NPS) specimen (i.e. specimen mixed with Sample Buffer) into the FilmArray RP pouch. The pouch contains all of the reagents required for specimen testing and analysis in a freeze-dried format; the addition of Hydration Solution and specimen/Sample Buffer Mix rehydrates the reagents. After the pouch is prepared, the FilmArray software guides the user though the steps of placing the pouch into the instrument, scanning the pouch barcode, entering the sample identification, and initiating the run.

The FilmArray instrument contains a coordinated system of inflatable bladders and seal points, which act on the pouch to control the movement of liquid between the pouch blisters. When a bladder is inflated over a reagent blister, it forces liquid from the blister into connecting channels. Alternatively, when a seal is placed over a connecting channel it acts as a valve to open or close a channel. In addition, electronically controlled pneumatic pistons are positioned over multiple plungers in order to deliver the rehydrated reagents into the blisters at the appropriate times. Two Peltier devices control heating and cooling of the pouch to drive the PCR reactions and the melt curve analysis.

Nucleic acid extraction occurs within the FilmArray pouch using mechanical and chemical lysis followed by purification using standard magnetic bead technology. After extracting and purifying nucleic acids from the unprocessed sample, a nested multiplex PCR is executed in two stages. During the first stage, a single, large volume, highly multiplexed reverse transcription PCR (rt-PCR) reaction is performed. The products from first stage PCR are then diluted and combined with a fresh, primer-free master mix and a fluorescent double stranded DNA binding dye (LC Green® Plus, BioFire Defense, LLC). The solution is then distributed to each well of the array. Array wells contain sets of primers designed specifically to amplify sequences internal to

the PCR products generated during the first stage PCR reaction. The 2nd stage PCR, or nested PCR, is performed in singleplex fashion in each well of the array. At the conclusion of the 2nd stage PCR, the array is interrogated by melt curve analysis for the detection of signature amplicons denoting the presence of specific targets. A digital camera placed in front of the array captures fluorescent images of the PCR reactions and software interprets the data.

The FilmArray software automatically interprets the results of each DNA melt curve analysis and combines the data with the results of the internal pouch controls to provide a test result for each organism on the panel.

Substantial Equivalence:

The FilmArray Respiratory Panel for use with FilmArray 2.0 and FilmArray Injection Vials is substantially equivalent to the FilmArray Respiratory Panel (K123620), which was cleared for use with the FilmArray on February 11, 2013 and determined to be a Class II device.

The following table compares the FilmArray Respiratory Panel for use with FilmArray 2.0 and FilmArray Injection Vials to the previously cleared FilmArray Respiratory Panel (K123620). The table outlines the similarities and differences between the two devices.

Table 2. Comparison of the FilmArray Respiratory Panel on FilmArray 2.0 and with FilmArray Injection Vials to the FilmArray Respiratory Panel on FilmArray (Predicate).

Element	Predicate: FilmArray Respiratory Panel (K123620)	New Device: FilmArray Respiratory Panel for use with FilmArray System 2.0 and FilmArray Injection Vials
Organisms Detected	Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype 2009 H1, Influenza B, Respiratory Syncytial Virus, Human Metapneumovirus, Adenovirus, Parainfluenza 1, Parainfluenza 2, Parainfluenza virus 3, Parainfluenza 4, Human Rhinovirus/Enterovirus, Coronavirus HKU1, Coronavirus NL63, Coronavirus 229E, Coronavirus OC43, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Bordetella pertussis*.	Same
Analyte	RNA/DNA	Same
Specimen Types	Nasopharyngeal swabs (NPS)	Same
Technological Principles	Nested multiplex RT-PCR followed by high resolution melting analysis to confirm identity of amplified product.	Same
Instrumentation	FilmArray	FilmArray or FilmArray System 2.0
Time to result	About 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same

Element	Predicate: FilmArray Respiratory Panel (K123620)	New Device: FilmArray Respiratory Panel for use with FilmArray System 2.0 and FilmArray Injection Vials
Reagent Hydration and Sample Loading	Syringe-based loading procedure	Syringe-based loading procedure or FilmArray Injection Vial-based loading procedure
Sample Preparation Method	Sample Processing is automated in the FilmArray RP pouch.	Same
Reagent Storage	Reagents are stored at room temperature.	Same
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis.	Same
User Complexity	Moderate/Low	Same

Summary of Performance Data

Clinical Performance

The original FilmArray Respiratory Panel was developed for use with the current, single instrument FilmArray and a syringe-based pouch loading procedure. A clinical study was conducted to compare the performance observed when testing clinical specimens using the FilmArray RP in its current configuration on the current system to results obtained when testing with the modified system using the current loading tools (platform comparison) as well as results on the modified platform when syringes or FilmArray Injection Vial loading tools are used (loading tools comparison). Data obtained with the current system/tools were also compared to the modified system with FilmArray Injection Vials (multifactor comparison).

Specimens previously obtained during the FilmArray RP prospective clinical evaluations comprised the base of the specimen set used for testing. This set was supplemented with other archived specimens collected from external medical facilities and reference laboratories to increase the number of specimens being tested for low prevalence analytes. A total of 102 specimens were selected such that each analyte was represented 3-5 times.

System performance for testing these 102 specimens on each platform was calculated. For the current system, a total of 108 runs were attempted, 104 of which were completed (96.3%; 104/108). There were two run failures each for software (1.9%) and instrument (1.9%) errors. No control failures were observed. Two specimens were retested due to Influenza A ‘equivocal’ results.

For the modified system (paired with syringe and FilmArray Injection Vial loading) a total of 205 runs were attempted, all of which were completed (100%; 205/205). There were no control failures. One specimen tested with the FilmArray Injection Vial loading tools was retested due to an Influenza A ‘equivocal’ result. All specimens were of sufficient volume that retesting was possible in order to obtain valid runs for all testing configurations.

As shown in Table 3, 100% concordance was observed for most analytes (13/20) across all comparisons. Occasional discrepant results were observed where an analyte was detected by one or two out of three runs; in all cases the discrepant results were attributed to analyte levels below the limit of detection (LoD) for a particular assay in specimens that had previously been characterized as positive for that analyte, or due to a known cross-reactivity (discussed further in Table 3). Overall Positive Percent Agreement (PPA) for all three comparisons was 96.8% or greater (100% for 16/20 analytes), with the lower bound of the two-sided 95% confidence interval (95% CI) at 92.0% or greater. Overall Negative Percent Agreement (NPA) for all three comparisons was 99.2% or greater (100% for 16/20 analytes), with the lower bound of the two-sided 95% CI at 99.5% or greater.

Table 3. Analyte Detections across all systems and loading tools. For all "X vs Y" headers, Y is the denominator. Comparisons demonstrating performance less than 100% are shaded. CS + S = Current System, Syringe; MS+S = Modified System, Syringe; MS+F = Modified System, FilmArray Injection Vial

Analyte	MS+S vs CS+S (System Comparison)				MS+F vs MS+S (Loading Tools Comparison)				MS+F vs CS+S (Multifactor Comparison)			
	PPA	%	NPA	%	PPA	%	NPA	%	PPA	%	NPA	%
Adenovirus	5/5	100%	97/97	100%	5/5	100%	97/97	100%	5/5	100%	97/97	100%
Coronavirus 229E	5/5	100%	97/97	100%	5/5	100%	97/97	100%	5/5	100%	97/97	100%
Coronavirus HKU1	6/6	100%	95/96[a]	99%	7/7	100%	95/95	100%	6/6	100%	95/96[a]	99%
Coronavirus NL63	6/6	100%	96/96	100%	6/6	100%	96/96	100%	6/6	100%	96/96	100%
Coronavirus OC43	4/5[b]	80%	97/97	100%	4/4	100%	98/98	100%	4/5[b]	80%	97/97	100%
Human Metapneumovirus	5/5	100%	97/97	100%	5/5	100%	97/97	100%	5/5	100%	97/97	100%
Human Rhinovirus/Enterovirus	8/10[c]	80%	92/92	100%	8/8	100%	92/94[c]	97.9%	9/10[c]	90%	91/92[c]	98.9%
Influenza A	16/16	100%	86/86	100%	16/16	100%	86/86	100%	16/16	100%	86/86	100%
Influenza A H1	3/3	100%	99/99	100%	3/3	100%	99/99	100%	3/3	100%	99/99	100%
Influenza A H1-2009	6/6	100%	96/96	100%	6/6	100%	96/96	100%	6/6	100%	96/96	100%
Influenza A H3	7/7	100%	95/95	100%	7/7	100%	95/95	100%	7/7	100%	95/95	100%
Influenza B	5/5	100%	97/97	100%	5/5	100%	97/97	100%	5/5	100%	97/97	100%
Parainfluenza Virus 1	7/7	100%	95/95	100%	7/7	100%	95/95	100%	7/7	100%	95/95	100%
Parainfluenza Virus 2	6/6	100%	96/96	100%	6/6	100%	95/96[d]	99%	6/6	100%	95/96[d]	99%
Parainfluenza Virus 3	6/6	100%	96/96	100%	6/6	100%	96/96	100%	6/6	100%	96/96	100%
Parainfluenza Virus 4	6/6	100%	96/96	100%	5/6[e]	83.3%	96/96	100%	5/6[e]	83.3%	96/96	100%
Respiratory Syncytial Virus	8/8	100%	94/94	100%	8/8	100%	94/94	100%	8/8	100%	94/94	100%
Bordetella pertussis	4/4	100%	98/98	100%	4/4	100%	97/98[f]	99%	4/4	100%	97/98[f]	99%
Chlamydophila pneumoniae	3/3	100%	99/99	100%	3/3	100%	99/99	100%	3/3	100%	99/99	100%
Mycoplasma pneumoniae	5/6[g]	83.3%	96/96	100%	5/5	100%	97/97	100%	5/6[g]	83.3%	96/96	100%
Overall Agreement	**121/125**	**96.8%**	**1914/1915**	**99.9%**	**121/122**	**99.2%**	**1914/1918**	**99.8%**	**121/125**	**96.8%**	**1911/1915**	**99.8%**
95% CI	**92.0-99.1%**		**99.7-100%**		**95.5-100%**		**99.5-99.9%**		**92.0-99.1%**		**99.5-99.9%**	

[a] Specimen 014111-RP-0037 was originally characterized as positive for CoV NL63 and was also unexpectedly positive for CoV HKU1 when tested on the MS+S and the MS+F but was not when tested on the CS+S.

[b] Specimen 014111-RP-0045 was originally characterized as positive for CoV HKU1 and demonstrated a known cross-reactivity with the CoV OC43 assay when tested with the CS+S only.

[c] Three specimens (014111-RP-0012, 014111-RP-0100, and 014111-RP-0101) demonstrated differential detection of HRV/EV across all testing configurations; HRV/EV had not been reported as present in these specimens by the source laboratory.
[d] Specimen 014111-RP-0091 was originally characterized as positive for CoV 229E and was also unexpectedly positive for PIV2 when tested on the MS+F but not when tested on the CS+S or MS+S.
[e] Specimen 014111-RP-0101 was originally characterized as positive for *B. pertussis* and was also unexpectedly positive for PIV4 when tested on the CS+S and the MS+S but was not when tested on the MS+F.
[f] Specimen 014111-RP-0097 was originally characterized as positive for *B. pertussis* and this analyte was detected when tested on the MS+F but was not detected when tested on the CS+S or MS+S.
[g] Specimen 014111-RP-0073 was originally characterized as positive for *M. pneumoniae* and this analyte was detected when tested on the CS+S but was not detected when tested on the MS+S or MS+F

Selected Analytical Studies

Low Analyte

A comparison of performance at low analyte levels between the current FilmArray system (one instrument to one computer configuration) and the FilmArray 2.0 system (modified; up to eight instruments to one computer) was performed for FilmArray RP. A comparison of performance between the current syringe-based pouch loading procedure and a modified, injection vial-based pouch loading procedure was also performed. The purpose was to establish that FilmArray RP performance is equivalent for all system and pouch loading combinations.

Testing consisted of a titration of samples containing RP analytes at concentrations above, at, and below (10×, 1×, 0.1× and 0.01×) LoD. Additional side-by-side testing at LoD (20 replicates on each system) was performed to further demonstrate consistency between the current (syringe) and modified (syringe or injection vial) system and pouch loading combinations.

In the titration series testing, amplification and detection of each analyte were found to be comparable between configurations at all concentrations. Testing of additional replicates at LoD (Table 4) also revealed equivalent detection on all three configurations (≥95% detection for the current and modified configurations and/or overlapping 2-sided 95% confidence intervals).

Table 4. Results of Replicate Testing at LoD for the Respiratory Panel (RP) on Current and Modified FilmArray Systems with Syringe and/or FilmArray Injection Vial Pouch Loading Procedures

Respiratory Panel Analyte	Current System (Syringe) # Detected % Positive [95% CI]	Modified System (Syringe) # Detected % Positive [95% CI]	Modified System (Injection Vial) # Detected % Positive [95% CI]
Adenovirus	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Bordetella pertussis	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Chlamydophila pneumoniae	19/20 **95%** [75.1-99.9%]	17/20 **85%**[a] [62.1-96.8%]	20/20 **100%** [83.2-100%]
Coronavirus 229E	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Coronavirus HKU1[b]	5-May **100%** [47.8-100%]	5-May **100%** [47.8-100%]	5-May **100%** [47.8-100%]
Coronavirus NL63	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Coronavirus OC43	19/20 **95%** [75.1-99.9%]	18/20 **90%**[a] [68.3-98.8%]	20/20 **100%** [83.2-100%]
Human Metapneumovirus	18/20	15/20	19/20

Respiratory Panel Analyte	Current System (Syringe) # Detected % Positive [95% CI]	Modified System (Syringe) # Detected % Positive [95% CI]	Modified System (Injection Vial) # Detected % Positive [95% CI]
	90%[a] [68.3-98.8%]	**75%**[a] [50.9-91.3%]	**95%** [75.1-99.9%]
Human Rhinovirus	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Enterovirus	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Influenza A H1	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Influenza A H1-2009	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Influenza A H3	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Influenza B	18/20 **90%**[a] [68.3-98.8%]	18/20 **90%**[a] [68.3-98.8%]	20/20 **100%** [83.2-100%]
Mycoplasma. pneumoniae	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Parainfluenza Virus 1	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Parainfluenza Virus 2	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]
Parainfluenza Virus 3	20/20 **100%** [83.2-100%]	19/20 **95%** [75.1-99.9%]	20/20 **100%** [83.2-100%]
Parainfluenza Virus 4	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	19/20 **95%** [75.1-99.9%]
Respiratory Syncytial Virus	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]	20/20 **100%** [83.2-100%]

[a] Detection rate is lower than the expected 95% at LoD, but detection is comparable between the current and modified configuration(s) and 95% confidence intervals are overlapping.
[b] Due to insufficient volume of Coronavirus HKU1, replicate testing was not performed. Results are from titration testing at LoD.

Tm values from the LoD replicate samples were compared to assess whether Tm data are equivalent between the current and modified FilmArray systems, the syringe and injection vial

pouch loading procedures, and between the current and modified system/loading combined. Normal Tm variation of the current FilmArray configuration is ±0.5˚C and it was observed that mean Tm values for all FilmArray RP assays on the modified configurations were ± 0.5°C or less compared to the same samples tested on the current configuration (ΔTm System, ΔTm Loading, and ΔTm Combined in Table 5).

Table 5. Comparison of Mean Tm Values for FilmArray RP Analytes on the Current and Modified Systems with Syringe or FilmArray Injection Vial Pouch Loading Procedures

Organism	Assay	Configuration	Mean Tm	ΔTm System	ΔTm Loading	ΔTm Combined
Control	PCR Control	Current (Syringe)	75.7	-0.1		0.0
		Modified (Syringe)	75.8		0.1	
		Modified (Injection Vial)	75.7			
	RNA Process Control	Current (Syringe)	81.7	0.1		0.1
		Modified (Syringe)	81.6		0.0	
		Modified (Injection Vial)	81.6			
Adenovirus	Adeno	Current (Syringe)	83.6	0.1		-0.2
		Modified (Syringe)	83.5		-0.3	
		Modified (Injection Vial)	83.8			
	Adeno2	Current (Syringe)	87.8	0.2		-0.3
		Modified (Syringe)	87.6		-0.5	
		Modified (Injection Vial)	88.1			
Bordetella pertussis	Bper	Current (Syringe)	88.1	-0.1		0.1
		Modified (Syringe)	88.2		0.2	
		Modified (Injection Vial)	88.0			
Chlamydophila pneumoniae	Cpne	Current (Syringe)	79.3	0		0.1
		Modified (Syringe)	79.3		0.1	
		Modified (Injection Vial)	79.2			
Coronavirus 229E	CoV-229E	Current (Syringe)	80.7	0.1		-0.3
		Modified (Syringe)	80.6		-0.4	
		Modified (Injection Vial)	81.0			
Coronavirus HKU1	CoV-HKU1	Current (Syringe)	75.2	0.1		0.2
		Modified (Syringe)	75.1		0.1	
		Modified (Injection Vial)	75.0			
Coronavirus NL63	CoV-NL63	Current (Syringe)	79.8	-0.1		0
		Modified (Syringe)	79.9		0.1	
		Modified (Injection Vial)	79.8			
Coronavirus OC43	CoV-OC43	Current (Syringe)	80.4	-0.1		0
		Modified (Syringe)	80.5		0.1	
		Modified (Injection Vial)	80.4			
Human Metapneumovirus	hMPV	Current (Syringe)	77.3	-0.2		0
		Modified (Syringe)	77.5		0.2	
		Modified (Injection Vial)	77.3			
Human Rhinovirus	HRV1	Current (Syringe)	83.5	0.2		0.1
		Modified (Syringe)	83.3		-0.1	
		Modified (Injection Vial)	83.4			
	HRV2	Current (Syringe)	83.4	0.2		0
		Modified (Syringe)	83.2		-0.2	
		Modified (Injection Vial)	83.4			
	HRV3	Current (Syringe)	82.8	0.2		-0.1

Organism	Assay	Configuration	Mean Tm	ΔTm System	ΔTm Loading	ΔTm Combined
		Modified (Syringe)	82.6		-0.3	
		Modified (Injection Vial)	82.9			
	HRV4	Current (Syringe)	83.8	0.3		0.3
		Modified (Syringe)	83.5		0	
		Modified (Injection Vial)	83.5			
Enterovirus	Entero1	Current (Syringe)	86.5	-0.1		0.1
		Modified (Syringe)	86.6		0.2	
		Modified (Injection Vial)	86.4			
	Entero2	Current (Syringe)	86.4	-0.2		0
		Modified (Syringe)	86.6		0.2	
		Modified (Injection Vial)	86.4			
	HRV3	Current (Syringe)	86.1	0.4		0.4
		Modified (Syringe)	85.7		0	
		Modified (Injection Vial)	85.7			
	HRV4	Current (Syringe)	85.2	-0.2		0
		Modified (Syringe)	85.4		0.2	
		Modified (Injection Vial)	85.2			
Influenza A H1	FluA-H1-pan	Current (Syringe)	78.0	0.2		0.1
		Modified (Syringe)	77.8		-0.1	
		Modified (Injection Vial)	77.9			
	FluA-pan1	Current (Syringe)	83.9	0.1		-0.3
		Modified (Syringe)	83.8		-0.4	
		Modified (Injection Vial)	84.2			
	FluA-pan2	Current (Syringe)	79.8	0.1		-0.2
		Modified (Syringe)	79.7		-0.3	
		Modified (Injection Vial)	80.0			
Influenza A H1-2009	FluA-H1-pan	Current (Syringe)	78.1	0.2		0.1
		Modified (Syringe)	77.9		-0.1	
		Modified (Injection Vial)	78.0			
	FluA-H1-2009	Current (Syringe)	78.5	0.3		-0.1
		Modified (Syringe)	78.2		-0.4	
		Modified (Injection Vial)	78.6			
	FluA-pan1	Current (Syringe)	84.5	0.2		-0.2
		Modified (Syringe)	84.3		-0.4	
		Modified (Injection Vial)	84.7			
	FluA-pan2	Current (Syringe)	80.3	0.3		-0.1
		Modified (Syringe)	80.0		-0.4	
		Modified (Injection Vial)	80.4			
Influenza A H3	FluA-H3	Current (Syringe)	81.9	-0.1		0
		Modified (Syringe)	82.0		0.1	
		Modified (Injection Vial)	81.9			
	FluA-pan1	Current (Syringe)	84.6	-0.2		0
		Modified (Syringe)	84.8		0.2	
		Modified (Injection Vial)	84.6			
	FluA-pan2	Current (Syringe)	79.2	-0.1		0
		Modified (Syringe)	79.3		0.1	
		Modified (Injection Vial)	79.2			
Influenza B	FluB	Current (Syringe)	79.8	0		0
		Modified (Syringe)	79.8		0	
		Modified (Injection Vial)	79.8			

Organism	Assay	Configuration	Mean Tm	ΔTm System	ΔTm Loading	ΔTm Combined
Mycoplasma pneumoniae	Mpne	Current (Syringe)	77.4	0.3		-0.1
		Modified (Syringe)	77.1		-0.4	
		Modified (Injection Vial)	77.5			
Parainfluenza Virus 1	PIV1	Current (Syringe)	78.0	0.1		-0.3
		Modified (Syringe)	77.9		-0.4	
		Modified (Injection Vial)	78.3			
Parainfluenza Virus 2	PIV2	Current (Syringe)	83.3	0.2		-0.2
		Modified (Syringe)	83.1		-0.4	
		Modified (Injection Vial)	83.5			
Parainfluenza Virus 3	PIV3	Current (Syringe)	80.7	-0.1		0
		Modified (Syringe)	80.8		0.1	
		Modified (Injection Vial)	80.7			
Parainfluenza Virus 4	PIV4	Current (Syringe)	76.9	-0.2		0.2
		Modified (Syringe)	77.1		0.4	
		Modified (Injection Vial)	76.7			
Respiratory Syncytial Virus	RSV	Current (Syringe)	80.4	0		-0.3
		Modified (Syringe)	80.4		-0.3	
		Modified (Injection Vial)	80.7			

Reproducibility

A multicenter reproducibility study was performed to determine between-site/system and overall reproducibility of the FilmArray Respiratory Panel (RP) on multi-instrument FilmArray 2.0 systems using the current (syringe) and modified (injection vial) pouch loading procedures.

Reproducibility testing occurred at three test sites using a panel of contrived nasopharyngeal swab samples, each spiked with various concentrations of four different RP analytes. Each analyte was evaluated at three different concentrations (Negative, Low Positive, and Moderate Positive).

The study incorporated a range of potential variation introduced by up to eight different operators, three different pouch lots, and up to 11 different FilmArray 2.0 instruments per loading procedure on three different systems. A system consisted of three instruments connected to a single computer. Samples were stored frozen and tested on five different days at three testing sites (one system, A, B, or C per site) for 90 data points per sample, per loading procedure.

A summary of results (percent (%) agreement with the expected result) for each analyte (by site/system and overall) is provided in Table 6 alongside the overall % Agreement with Expected Results originally obtained on the single-instrument system.

Table 6. Reproducibility of the FilmArray Respiratory Panel Test Results on FilmArray 2.0 (Multi-instrument) and FilmArray (Single-instrument)

Organism Tested	Concentration Tested	Expected Result	% Agreement with Expected Result[a]								
			Multi-instrument + Syringe				Multi-instrument + Injection Vial				Single-instrument + Syringe
			Site/System			All Sites/ Systems (95% Confidence Interval)	Site/System			All Sites/ Systems (95% Confidence Interval)	All Sites (95% Confidence Interval)
			A	B	C		A	B	C		
***Bordetella pertussis* Strain A639** Zeptometrix 0801459	**Moderate Positive** 3× LoD $1.2x10^4$ CFU/mL	Detected	29/29[a] 100%	30/30 100%	30/30 100%	89/89[a] 100% (95.9-100%)	30/30 100%	29/30 96.7%	30/30 100%	89/90 98.9% (94.0-100%)	60/60 100% (94.0-100%)
	Low Positive 1× LoD $4x10^3$ CFU/mL	Detected	29/30 96.7%	30/30 100%	27/30 90.0%	86/90 95.6% (89.0-98.8%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	60/60 100% (94.0-100%)
	Negative	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	540/540 100% (99.3-100%)
Adenovirus Species C Serotype 1 Zeptometrix 0810050CF	**Moderate Positive** 3× LoD $3.0x10^2$ $TCID_{50}$/mL	Detected	30/30 100%	30/30 100%	28/30 93.3%	88/90 97.8% (92.2%-99.7%)	29/30 96.7%	30/30 100%	30/30 100%	89/90 98.9% (94.0-100%)	60/60 100% (94.0-100%)
	Low Positive 1× LoD $1.0x10^2$ $TCID_{50}$/mL	Detected	28/29[a] 96.6%	30/30 100%	28/30 93.3%	86/89[a] 96.6% (90.5%-99.3%)	30/30 100%	30/30 100%	29/30 96.7%	89/90 98.9% (94.0-100%)	60/60 100% (94.0-100%)
	Negative	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	540/540 100% (99.3-100%)
Influenza A H1N1-2009 A/SwineNY/ 03/2009 Zeptometrix 0810109CFN	**Moderate Positive** 3× LoD $3.0x10^2$ $TCID_{50}$/mL	Detected	29/29[a] 100%	30/30 100%	30/30 100%	89/89[a] 100% (95.9-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	60/60 100% (94.0-100%)
	Low Positive 1× LoD $1.0x10^2$ $TCID_{50}$/mL	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	60/60 100% (94.0-100%)
	Negative	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	540/540 100% (99.3-100%)
Respiratory Syncytial Virus Type A Zeptometrix 0810040ACF	**Moderate Positive** 3× LoD 6.0 $TCID_{50}$/mL	Detected	30/30 100%	30/30 100%	30/30 100%	90/90% 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	180/180 100% (98.0-100%)
	Low Positive 1× LoD 2.0 $TCID_{50}$/mL	Detected	29/29[a] 100%	30/30 100%	30/30 100%	89/89[a] 100% (95.9-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	120/120 100% (97.0-100%)
	Negative	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	30/30 100%	30/30 100%	30/30 100%	90/90 100% (96.0-100%)	360/360 100% (99.0-100%)

[a] Due to failure, a valid result could not be obtained for one of the replicates, reducing the total number of replicates for Site/System A from 30 to 29 and for All Sites/Systems from 90 to 89.

The test results obtained for the FilmArray Respiratory Panel on FilmArray 2.0 following the syringe and injection vial loading procedures were highly reproducible and are consistent with the data collected on the current, single-instrument FilmArray in the original FilmArray RP Reproducibility evaluation.

The reproducibility of Tm for each positive assay was also evaluated by site/system and overall (all sites/systems) and a summary is provided in Table 7.

Table 7. Reproducibility of Tm for Positive FilmArray RP Assays on Multi-instrument FilmArray 2.0 Systems

Organism	Assay	Test Level	Site/System	Tm Reproducibility			
				Syringe		Injection Vial	
				Mean	StDev Tm	Mean	StDev Tm
Bacteria							
Bordatella pertusis Zeptometrix 0810050CF	**Bper**	**Moderate Pos 3× LoD 1.2x10^4 CFU/mL**	**A**	88.3	±0.3	88.3	±0.2
			B	88.2	±0.2	88.1	±0.2
			C	87.8	±0.4	88.0	±0.2
			All Sites/Systems	88.1	±0.4	88.1	±0.3
		Low Pos 1× LoD 4.0x10^3 CFU/mL	**A**	88.3	±0.2	88.4	±0.2
			B	88.2	±0.2	88.1	±0.2
			C	87.8	±0.4	88.0	±0.2
			All Sites/Systems	88.1	±0.3	88.2	±0.2
Viruses							
Influenza A H1-2009 Zeptometrix 0810109CFN	**FluA-H1-2009**	**Mod Pos 3× LoD 300 TCID$_{50}$/mL**	**A**	78.6	±0.2	78.6	±0.2
			B	78.5	±0.2	78.4	±0.2
			C	78.1	±0.3	78.2	±0.2
			All Sites/Systems	78.4	±0.3	78.4	±0.3
		Low Pos 1× LoD 100 TCID$_{50}$/mL	**A**	78.6	±0.2	78.6	±0.2
			B	78.5	±0.2	78.5	±0.2
			C	78.2	±0.3	78.3	±0.2
			All Sites/Systems	78.4	±0.3	78.5	±0.2
	FluA-H1-pan	**Mod Pos 3× LoD 300 TCID$_{50}$/mL**	**A**	78.1	±0.2	77.9	±0.2
			B	78.1	±0.2	77.9	±0.3
			C	77.7	±0.3	77.7	±0.3
			All Sites/Systems	77.9	±0.3	77.8	±0.3
		Low Pos 1× LoD 100 TCID$_{50}$/mL	**A**	78.4	±0.3	78.2	±0.4
			B	78.4	±0.4	78.1	±0.3
			C	78.0	±0.5	77.9	±0.3
			All Sites/Systems	78.3	±0.4	78.1	±0.3
	FluA-pan1	**Mod Pos 3× LoD 300 TCID$_{50}$/mL**	**A**	84.9	±0.2	84.9	±0.2
			B	84.7	±0.2	84.6	±0.2
			C	84.4	±0.3	84.5	±0.2
			All Sites/Systems	84.7	±0.3	84.7	±0.2

Organism	Assay	Test Level	Site/System	Tm Reproducibility			
				Syringe		Injection Vial	
				Mean	StDev Tm	Mean	StDev Tm
		Low Pos 1× LoD 100 $TCID_{50}$/mL	**A**	84.9	±0.2	84.9	±0.2
			B	84.7	±0.2	84.7	±0.2
			C	84.4	±0.3	84.6	±0.1
			All Sites/Systems	84.7	±0.3	84.7	±0.2
	FluA-pan2	**Mod Pos 3× LoD 300 $TCID_{50}$/mL**	**A**	80.4	±0.2	80.2	±0.4
			B	80.4	±0.1	80.1	±0.2
			C	80.1	±0.3	80.2	±0.2
			All Sites/Systems	80.3	±0.3	80.2	±0.3
		Low Pos 1× LoD 100 $TCID_{50}$/mL	**A**	80.5	±0.2	80.4	±0.3
			B	80.5	±0.2	80.3	±0.2
			C	80.2	±0.3	80.2	±0.2
			All Sites/Systems	80.4	±0.3	80.3	±0.2
Adenovirus Zeptometrix 0810050CF	**Adeno**	**Mod Pos 3× LoD 300 $TCID_{50}$/mL**	**A**	83.7	±0.3	83.8	±0.3
			B	83.6	±0.3	83.4	±0.3
			C	83.4	±0.4	83.4	±0.3
			All Sites/Systems	83.6	±0.4	83.5	±0.3
		Low Pos 1× LoD 100 $TCID_{50}$/mL	**A**	84.0	±0.3	84.0	±0.3
			B	83.9	±0.3	83.6	±0.3
			C	83.7	±0.4	83.6	±0.3
			All Sites/Systems	83.9	±0.3	83.8	±0.3
	Adeno2	**Mod Pos 3× LoD 300 $TCID_{50}$/mL**	**A**	88.1	±0.2	88.2	±0.3
			B	87.9	±0.2	87.9	±0.2
			C	87.7	±0.4	87.8	±0.2
			All Sites/Systems	87.9	±0.3	88.0	±0.3
		Low Pos 1× LoD 100 $TCID_{50}$/mL	**A**	88.2	±0.3	88.2	±0.2
			B	88.1	±0.1	87.9	±0.3
			C	87.8	±0.4	87.8	±0.2
			All Sites/Systems	88.0	±0.3	88.0	±0.3
Respiratory Syncytial Virus Zeptometrix 0810040ACF	**RSV**	**Mod Pos 3× LoD 6 $TCID_{50}$/mL**	**A**	80.8	±0.3	80.6	±0.5
			B	80.7	±0.3	80.6	±0.3
			C	80.4	±0.3	80.6	±0.2
			All Sites/Systems	80.6	±0.3	80.6	±0.4
		Low Pos 1× LoD 2 $TCID_{50}$/mL	**A**	80.8	±0.2	80.6	±0.5
			B	80.8	±0.2	80.6	±0.3
			C	80.5	±0.3	80.6	±0.2
			All Sites/Systems	80.7	±0.3	80.6	±0.3